Analog Natural Diseases
for Biological Effects of Lunar Dust

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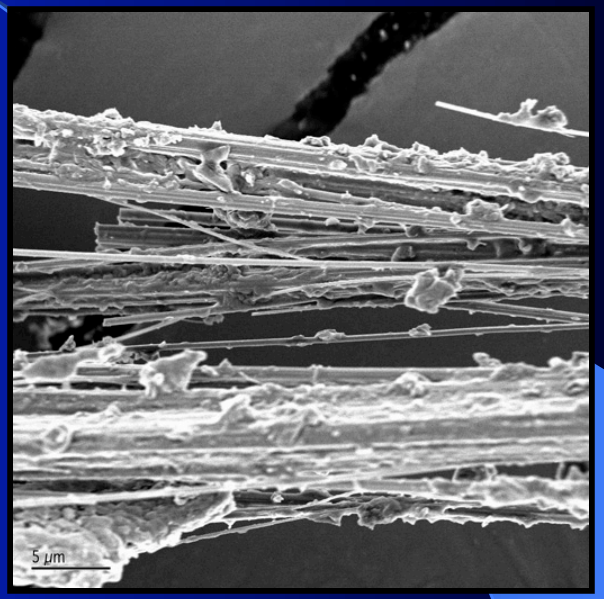
Analog Natural Diseases:
Asbestos-Related

- *Pneumoconiosis*
  - General term for lung disease caused by inhalation and deposition of mineral dust.
  - Can result in crippling or fatal pulmonary fibrosis or malignancy
  - Primarily industrial diseases, although known to occur rarely in nature due to mineral deposits
  - Big Three: Asbestosis, Coal Worker's Lung, and Silicosis
  - Many others: talc, kaolin, siderosis (iron), barium, tin, cobalt, tungsten carbide, titanium oxide, Zeolite, carbon nano-tubes (?).

Analog Natural Diseases:
Asbestos-Related



- Asbestos related disease:
  - "inextinguishable" [Greek]
  - Asbestos is a group of naturally occurring, heat-resistant fibrous silicates
  - Associated with fibrosis and malignancy
  - Risk of malignancy is related to exposure to long fibers (> 10 microns)
  - Toxicity is a complex function of the fiber dose, dimensions, durability, and other factors widely documented in the scientific literature.

Analog Natural Diseases:
Asbestos-Related

- Mesothelioma
- Most famous victim: **Steve McQueen**
  - surrounded by asbestos all his life
  - odd jobs-at construction sites
  - found on movie sound stages
  - brake linings of race cars
  - in the race car helmets and suits
- While in the Marines in the Aleutian Islands got thrown in the brig and was put on work detail in the hold of a ship. Was exposed to an extremely high dose of asbestos fibers. “The air was so thick with asbestos particles, that the men could hardly breathe…”

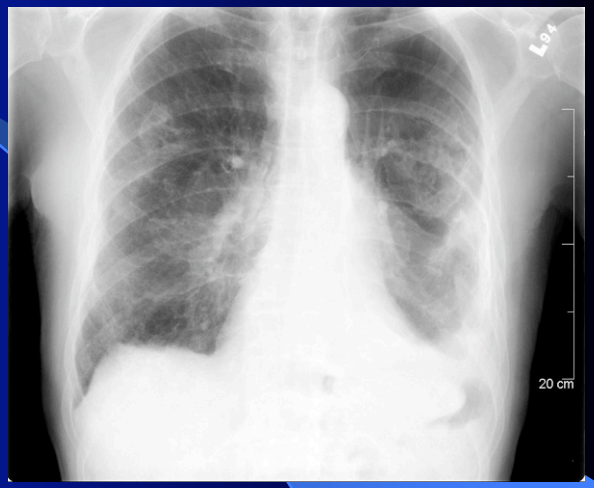
Analog Natural Diseases:
Asbestos-Related

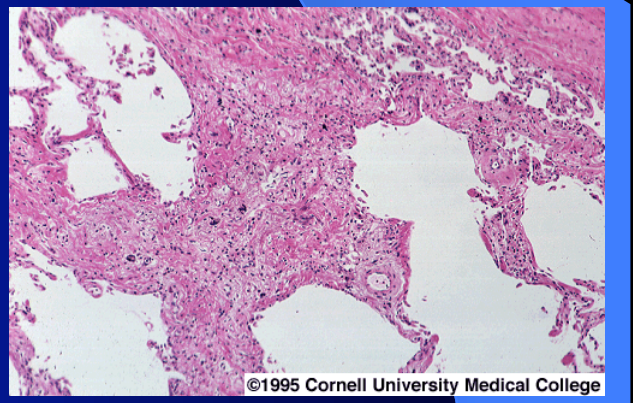
- Exposure of the general population:
  - Some commercial talcum powder was over 50% asbestos fibers (& talc itself can cause a serious pneumoconiosis)
  - Brake linings
  - Ceiling & floor tiles
  - Fire-proofing materials
  - Home insulation: electrical, etc.
  - Secondary exposure
  - Natural exposure: Serpentine, the State Rock of California, contains asbestos

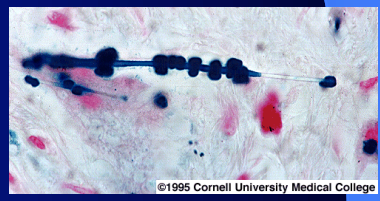
Analog Natural Diseases:

Asbestos-Related

- Asbestosis Pathophysiology:
  - Asbestosis is a progressive fibrosis of the interstitial space of the lung.
  - We all have asbestos fibers in our lungs.
  - In quantity, all types of asbestos fibers are fibrogenic to the lungs.
  - Fibers with diameters smaller than 3 micrometers are most fibrogenic because they penetrate cell membranes.
  - **Long fibers (ie, >5 micrometers) are incompletely phagocytized and stay in the lungs, setting up cycles of cellular events and the release of cytokines and generate oxygen free radicals that damage proteins, etc., perpetuating the inflammatory response.**
  - Individuals differ in susceptibility based on respiratory clearance and other unidentified host factors.
  - Symptoms may appear only after a latent period of 20 years or longer. This latent period may be shorter after intense exposure.

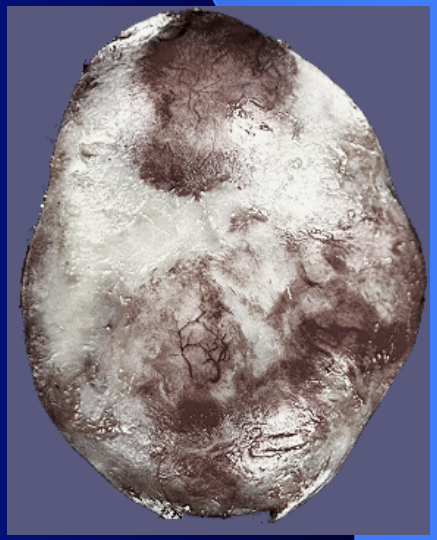






Analog Natural Diseases:
Asbestos-Related

- Malignancy: Fiber micromorphology and risk.
  - McDonald et.al. 1989: Risk of mesothelioma related to amphibole fibers longer than 8 µm; fibers shorter than 8 µm accounted for none of the cancer risk
  - Rogers et al. 1991: Mesothelioma risk was greatest for crocidolite asbestos fibers longer than 10 µm, followed by amosite asbestos fibers longer than 10 µm, and then by chrysotile fibers less than 10 µm (suspected risk for chrysotile fibers < 10 µm resulted from longer fibers breaking into shorter fibers)
  - Rödelsperger et al. 1999: 66 individuals died from mesothelioma "...a clear dose-response relationship up to an odds ratio of 99% has been demonstrated for the lung tissue concentration of total amphibole fibers longer than 5 µm."

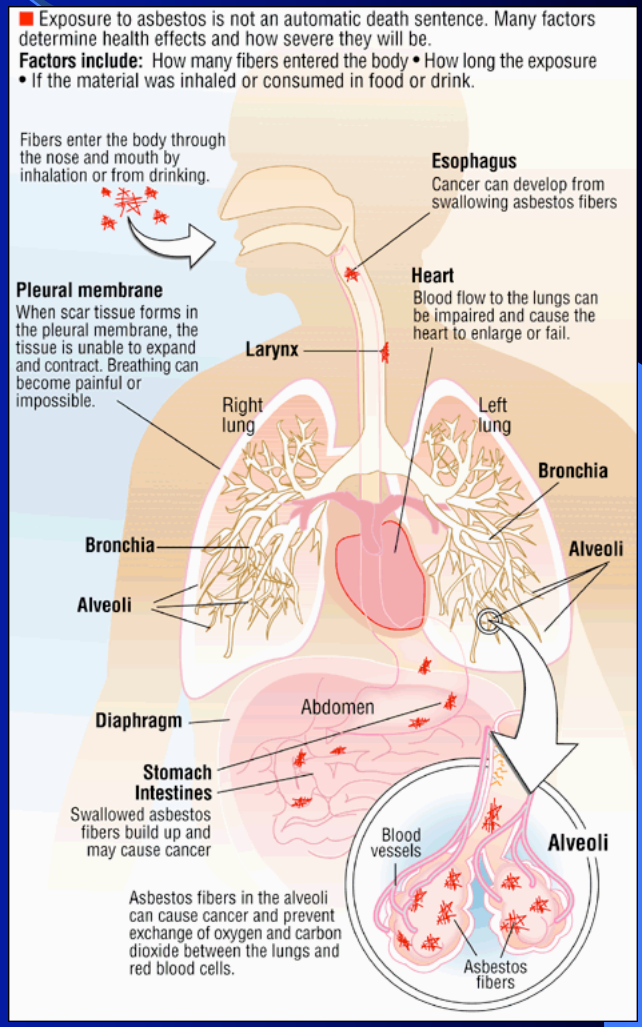


Analog Natural Diseases:
Asbestos-Related

- Extensive lung tissue sampling and other highly invasive tests in humans are only feasible at autopsy: How relevant are animal studies?
- **Report on the Expert Panel on Health Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length** (Agency on Toxic Substances and Disease Registry, 2003)
- Utility of laboratory animal studies for understanding toxicity of asbestos and SVFs.
  - Benefits:
    - conduct highly controlled experiments using well-defined exposure levels
    - evaluate health outcomes and lung-retention levels at many different time frames following exposure
    - the rat has been shown to develop both mesothelioma and lung cancer, though not as aggressive in the rat as in humans
    - [KC-135 and other flight experiments, higher N]
  - Factors and differences:
    - life span
    - macrophage size
    - airway branching patterns
    - relevancy of high dose and administration methods (e.g., peritoneal injection vs. inhalation of aerosol)
    - failure to address certain human exposure conditions (e.g., smoking).
- Overall, after analysis of supportive scientific studies, the panelists agreed that laboratory animal studies can provide useful insights into toxicity to humans.
- Asbestos simulants (Synthetic Vitreous Fibers) may be useful in experimental studies.

Analog Natural Diseases:
Asbestos-Related

- Other organs affected
  - Eyes
    - Irritation
    - Corneal abrasion
  - Upper airway
    - Hay fever-like symptoms
    - Carcinoma (controversial)
  - GI malignancy
    - Esophagus (controversial)
    - Intestines (controversial)



Analog Natural Diseases:
Coal Worker's Lung

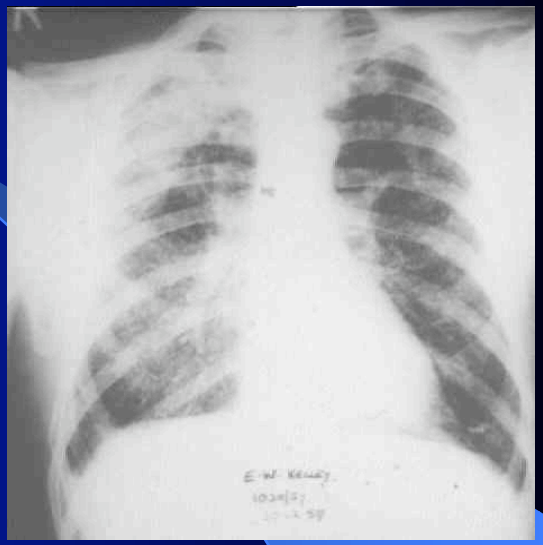
- Coal Worker's Pneumoconiosis (CWP; Coal Worker's Lung; "Black Lung" [legal term])
  - Black fibrotic lesions with cavitation in the lungs of coal miners
  - Historically, significant coincidence with silicosis confused analysis
  - Pure coal dust was thought to be innocuous, even beneficial
  - Epidemiological data showed disease generated by coal that had been washed free of silica
  - Graphite industry workers get CWP
  - 2/3 of U.S. coal is strip-mined, which results in less exposure

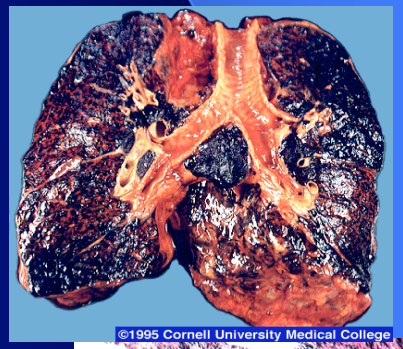
Analog Natural Diseases:

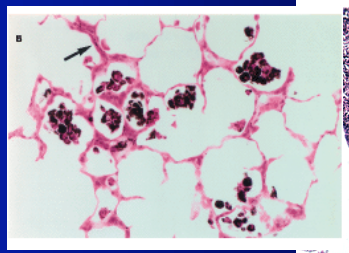
Coal Worker's Lung

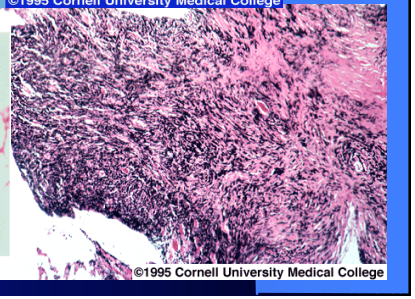
Analog Natural Diseases:
Coal Worker's Lung

- CWP Pathophysiology:
  - Disease results from host response to coal dust in lung.
  - Pure carbon is relatively inert and large quantities are required
  - Alveolar macrophages become glutted with carbon and lose function ("overload hypothesis")
  - CXR shows rounded densities in upper lung fields; can mimic cancer
  - Simple CWP usually asymptomatic
  - Complicated CWP assoc. disability and death, leads to pulmonary fibrosis, restrictive effects, and cardiac failure



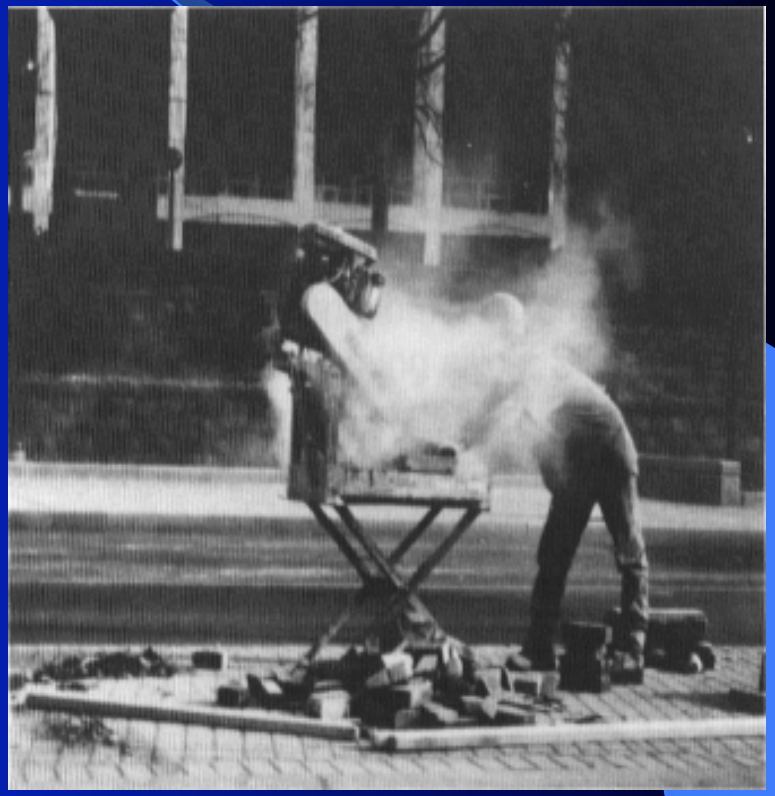






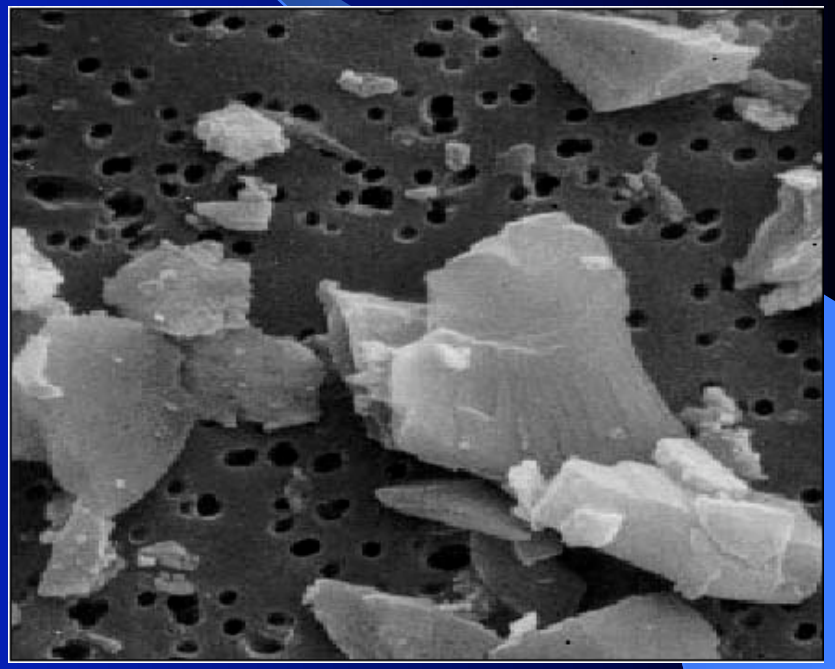
Analog Natural Diseases:
Silicosis

- Silicosis
  - Known for millennia: “Stone cutter’s disease”. Seen in Egyptian mummies.
  - Still seen in underdeveloped countries and sporadically elsewhere.
  - Free crystalline silica, usually quartz found in sand, sandstone, slate, some clays, granite, etc.
  - Sandblasters, miners, tunnel builders, quarry workers, foundry workers, ceramics and glass workers, and many other industries



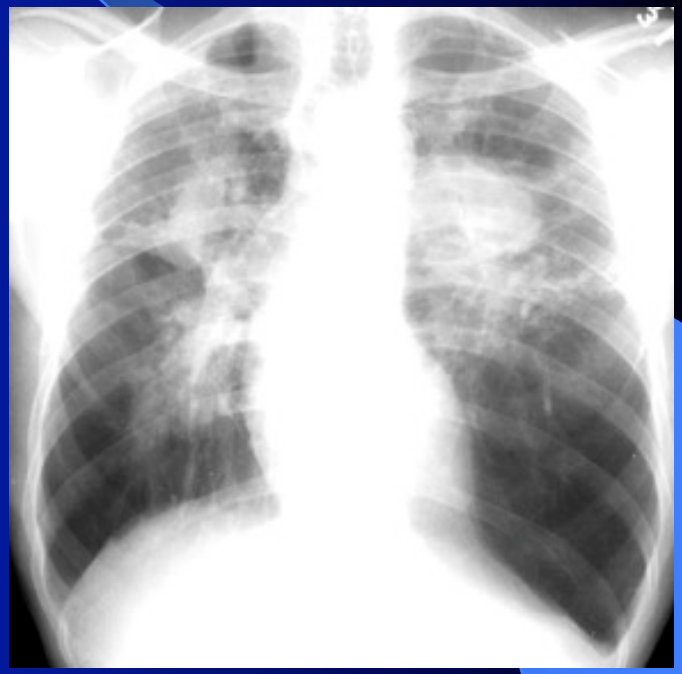
Analog Natural Diseases:
Silicosis

- Relevant Mineralogy
  - Quartz, tridymite, cristobalite, coesite, all have tetrahedral arrangement of Si04 groups and are highly fibrogenic
  - Stishovite is octahedral, and is not fibrogenic
  - Stishovite and Coesite are found naturally in meteorite craters
  - Amorphous silica is non-fibrogenic, but may become so when heated to crystalline forms
  - Particles less than 1 micron are the most fibrogenic
  - Sharp-edged morphology



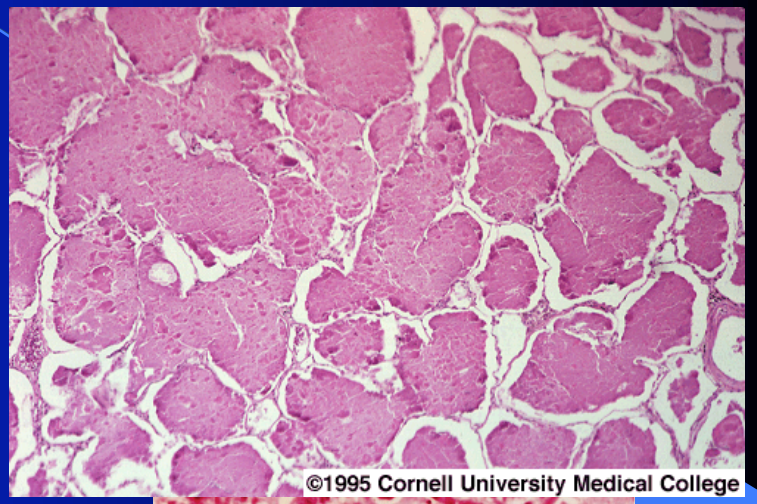
Analog Natural Diseases:
Silicosis

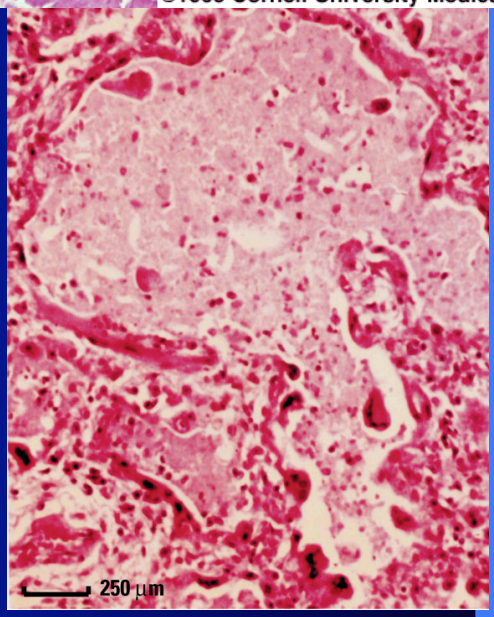
- Silicosis Pathophysiology
  - Particles ingested by alveolar macrophages and attract neutrophils
  - Macrophages rupture and die, releasing inflammatory mediators and recycling the particle
  - Particles may enter the interstitium, where they induce fibrosis
  - Silanol (SiOH) groups on surface of particles may react with cell membranes
  - Negative surface charge on SiO- groups may underlie direct toxicity
  - Freshly fractured silica contains more surface radicals causing more cell membrane damage than aged silica and is more potent in stimulating macrophages to produce oxidant species such as peroxide.
  - Fibrosis can become progressive and self-sustaining, but may still take 20 years to show on Xrays.
  - Clinical silicosis usually becomes evident 20-40 years after exposure
  - Patients usually die of tuberculosis or other superimposed disorder, not from the chronic silicosis itself
  - The weight of evidence is against a carcinogenic role for uncombined silicon dioxide



Analog Natural Diseases:
Silicosis

- Acute Silicoproteinosis
  - A relatively rapid onset form of toxic reaction to free silica
  - Very different than classical chronic fibrosing silicosis
  - Usually seen within 3 years of exposure to high concentrations of relatively fine silica
  - Can occur with exposures to dust for as little as 2-3 months
  - Characterized by breakdown of blood barrier and entry of blood plasma proteins into pulmonary air spaces
  - Alveolar proteinosis – a non-specific reaction also seen with fungal infections and other toxins
  - High mortality rate – rapidly fatal
  - Cause of death of most of the Hawks Nest Tunnel disaster victims





What Can we Learn about Lunar Dust from Terrestrial Pneumoconioses?

- The genesis of human disease is exquisitely sensitive to the specific micromorphology and microchemistry of dust grains
- Diseases may occur from a few years to decades after exposure
- Exposures as short as 2-3 months may cause disease
- Toxicity depends on complex combination: total dose, grain dimensions, chemistry, durability, host factors, exposure profile
- ALS/EVA mitigation strategies must be based on thorough knowledge of lunar dust subcomponent toxicity
- Simulants must have very high fidelity and be toxicologically validated against actual lunar dust samples
- Lunar dust is an entirely new type of mineral dust hazard requiring respect and careful study

References

- Report on the Expert Panel on Health Effects of Asbestos and Synthetic Vitreous Fibers: The Influence of Fiber Length (Agency on Toxic Substances and Disease Registry, 2003) http://www.atsdr.cdc.gov/HAC/asbestospanel/asbestostoc.html
- Pathology of Occupational Lung Disease Andrew Churg, M.D. & Francis Green, M.D. 2nd ed. Williams & Wilkins 1998